UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/035,045	01/03/2002	Jon Elliot Adler	P 280681 2001-019	3276

7590 12/15/2004

CROWELL & MORING LLP
P O BOX 14300
WASHINGTON, DC 20044-4300

EXAMINER	
BRANNOCK, MICHAEL T	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 12/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/035,045	ADLER ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-234* is/are pending in the application.

4a) Of the above claim(s) *120-198 and 223-234* is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-11,14-41,44-51,56-63,66-119,201-208 and 211-222* is/are rejected.

7)☒ Claim(s) *12,13,42,43,52-55,64,65,199,200,209 and 210* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 April 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *072604*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application: Claims and Amendments

Claims 120-198, 223-234 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 9/30/04.

Applicant's election with traverse of Group I, claims 1-199, 132-148, 150, 151, 177-222 as the claims relate to the elected species of hT1R2 is acknowledged. However, the examiner finds that only claims 1-119, 199-222 read on the elected species.

The traversal is on the grounds that polynucleotide claims and encoded polypeptide claims should be examined together and that a search of both would not be a serious burden on the examiner. This is not found persuasive for the following reasons:
Under MPEP § 803, there are two criteria for a proper requirement for restriction between patentably distinct inventions:

(A) The inventions must be independent (see MPEP § 8702.01, 806.04, 808.01) or distinct as claimed (see MPEP § 806.05- §806.05(I)): and
(B) There must be a serious burden on the examiner if restriction is required (see MPEP § 803.02, § 806.04(a)- 806.04(I), § 808.01(a), and § 808.02).

Consistent with current patent practice, a serious search burden may be established by (A) separate classification thereof: (B) a separate status in the art when they are classifiable together: (C) a different field of search. These criteria were met in the above restriction. Further, a search is directed not only to art which would be anticipatory, but also to art that would render the invention obvious. In the instant case, although a search of the polypeptides of Group II would overlap a search of the polynucleotides of Group I, the two searches would not

be coextensive. In many instances, a protein will have been known in the art before the DNA has been discovered that encodes the protein. Often the protein will be known by a name different than the name given the protein after the cloning of the nucleic acid - and may even be associated with a completely different activity than that ascribed to it when the nucleic acid was cloned. Thus, Groups I and II require divergent searches, and to search both inventions would be burdensome. Therefore, the restriction is maintained and made final

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, see pages 16 and 39 for example. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Additionally, the disclosure is objected to because the US Provisional Application Number at Page 10 is left blank. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 10, 11, 14, 15, 24, 25, 34, 35, 44, 45, 56-58, 68, 69, 80, 81, 90-119 201, 202, 213, 214 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 90, 103 and dependent claims, require a "variant" of a DNA. The word "variant" is used in the art to denote a relative relationship between two things, yet the specification has not set forth a clear distinction between what is to be considered a "variant" and what is considered to be unrelated. Thus, the artisan could not unambiguously know whether or not he or she was in possession of polynucleotides that are encompassed by Applicants claims. Additionally, claim 103 requires a "variant molecule". The sentence structures of the claims do not explicitly set forth what reference molecule the claimed variant molecule is a variation of, therefore the metes and bounds of the claim cannot be determined.

Claim 2 recites the phrase "consists essential of SEQ ID NO: 15 or 20". This appears to be a minor typographical error, however the phrase renders the claims indefinite because the artisan cannot determine what is and what is not being claimed. For the purpose of this examination, it is assumed that Applicant intended the phrase to read "consisting essentially of".

Claims 4, 5, 14, 15, 24, 25, 34, 35, 44, 45, 56, 57, 68, 69, 80, 81, 92, 93, 105, 106, 201, 202, 213, 214, require that the nucleic acid hybridize under stringent conditions. The term "stringent conditions" is a relative term and encompasses conditions of varying degrees of stringency - such conditions determining the bounds of the claim. However, the art does not provide an unambiguous definition of the term "stringent conditions" and neither is such a definition given for the term in the specification which puts forth the metes and bounds of the claim Applicant is seeking protection for. The term appears to be defined only by way of example at page 30. It is suggested that the claim recite the actual conditions that applicant considers to be stringent, e.g., salt concentration and temperature conditions of incubations and washes.

Claim 58 requires an isolated fragment "of the genomic DNA molecule of claim 54", yet there is no genomic DNA molecule of claim 54, thus the artisan would not know which genomic DNA molecule the claim is referring to.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-11, 14-41, 44-51, 56-119, 201-208, 211-222 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated naturally occurring polynucleotides that hybridize to a polynucleotide of SEQ ID NO: 20 under the stringent conditions set forth in lines 17 and 18 of page 16 of the specification and encode a polypeptide that bind sucrose in conjunction with a T1R3 polypeptide, does not reasonably provide enablement for artificially constructed polynucleotides that encode variants of the polypeptide of SEQ ID NO: 21, and nor for fragments of the polynucleotide of SEQ ID NO: 20. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims encompass polynucleotides encoding polypeptide variants of the polypeptide of SEQ ID NO: 21, i.e. substitutions, deletions or insertions in a protein corresponding to SEQ ID NO: 21 Applicant has not provided sufficient guidance as to how to make and use the encoded polypeptides which are not 100% identical to the polypeptide of SEQ ID NO: 21, but which still retain a desired property of the polypeptide of SEQ ID NO: 21.

The specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make. Furthermore, Applicant has not provided guidance as to what properties of the allelic variants or sequence variants of the protein corresponding to SEQ ID NO: 4 might be desired nor any guidance as to which amino acid substitutions, deletions or insertions to make to achieve any desired property. Applicant has not defined a difference in structure or difference in function between the protein corresponding to SEQ ID NO: 21 and variants of said protein. If a variant of the protein corresponding to SEQ ID NO: 21 is to have a structure and function similar to the protein corresponding to SEQ ID NO: 21 then the specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make that will preserve the structure and function of the protein corresponding to SEQ ID NO: 21.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see Bowie et al., 1990, Science 247:1306-1310, especially p.1306, column 2, paragraph 2). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art

to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Also, these or other regions may be critical determinants of antigenicity. It is well appreciated in the art of antibody production that it is unpredictable which amino acids are critical antigenic determinants (see Alexander et al., Proc. Natl. Acad. Sci. 89(3352-3356)1992. Protein antigenicity can be significantly reduced by substitution of even a single residue. Further, even if an amino acid substitution does not destroy the activity of the immunizing protein, the substitution may significantly reduce the antigenicity of the protein (see the Abstract of Alexander et al.). The specification does not provide sufficient guidance as to how to make antibodies that are specific to variants of SEQ ID NO: 21 that can be used for any specific purpose. The specification has not provided guidance as to natural variants that may exist, nor how to use antibodies specific to variants that might be created.

Although the specification outlines art-recognized procedures for producing variants, this is not adequate guidance as to the nature of active variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity.

The problem of producing active variants appears especially difficult in the art of T1R receptors, to which the instant polypeptide is asserted to belong. The instant specification

appears to simply suggest to the artisan that art-recognized procedures for screening GPCRs (e.g. pages 32-33, 40 and the example at page 91) are sufficient to identify functional variants of SEQ ID NO: 21. However, Hoon *et al., Cell* 96(541-551)1999, report that "We have attempted to determine the ligand/tastant specificity of TR1 and TR2 using a variety of strategies but have been hampered by the difficulty of functionally expressing these molecules in heterologous systems" see col 1 of page 547. The art regarding T1R receptors, as exemplified by Hoon et al., recognizes the complexity, unpredictability, and non-routine nature of the work involved in trying to assay functional T1R receptors. The instant specification has provided only general guidance to the skilled artisan -such guidance does not supply the artisan with the detailed methods one would need to possess in order to screen for functional variants. Further, the specification has offered no working example of such variants

Additionally, the specification has provide no specific information as to which of multitude of the small fragments of DNA, e.g. claim 6, can be used for any specific purpose.

Therefore, due to the large quantity of experimentation necessary to generate the infinite number of variant recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function and the difficulties encountered in screening T1Rs, exemplified by Hoon et al., and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 1, 4, 5, 7-11, 14, 15, 17-41, 44, 45, 47-53, 56, 57, 59-119, 201, 202, 204-208, 211-222 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses a naturally occurring polynucleotide of SEQ ID NO: 20 encoding a polypeptide of SEQ ID NO: 21, yet the claims encompass polynucleotides not described in the specification, e.g., artificially mutated sequences, sequences that have a recited degree of identity or that merely hybridize to SEQ ID NO: 20. These claimed genera do not meet the written description provision of 35 U.S.C. 112, first paragraph. Although one of skill in the art would reasonably predict that these sequences exist or could be made to exist, one would not be able make useful predictions as to the nucleotide positions or identities of those sequences based on the information disclosed in the specification.

A genus claim may be supported by a representative number of species as set forth in Regents of the University of California v Eli Lilly & Co, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses no artificially mutated sequences that have any function. Further, even if the disclose sequence were definitive of a genus with a specified function, the instantly claimed genus is not so limited

and the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify/obtain the polynucleotides encompassed, thus the artisan would not consider Applicant to be in possession of the breadth that is claimed.

With the exception of the of the polynucleotide of SEQ ID NO: 20, the skilled artisan cannot envision the detailed chemical structure of the encompassed variants. Therefore, only the polynucleotide of SEQ ID NO: 20 , other polynucleotides that encode a polypeptide of SEQ ID NO: 21, and polynucleotides consisting of fragments thereof, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 6, 14-16, 22-26, 32-36, 44, 45, 56, 57, 66-70, 76-82, 88-94, 100-107, 113-118, 201-203, 211-215, 221, 222 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoon *et al., Cell* 96(541-551), February 19, 1999.

Hoon et al. disclose a polynucleotide encoding a polypeptide with over 70% sequence identity with the instant SEQ ID NO: 20, see attached sequence alignment, and would thus be expected to hybridize under what could be considered stringent hybridization conditions as stated in the claims, absent evidence to the contrary. Isolated RNA is also described, page 542. PCR primers are disclosed, page 544, which would meet the conditions of being between about 20-30 nucleotide bases in length, absent evidence to the contrary.

Claims 7-11, 17-21, 27-31, 37-41, 47-51, 59-63, 71-75, 83-87, 95-99, 103-115, 204-208, 216-220 are rejected under 35 U.S.C. 102(b) as being anticipated by Krautwurst et al. Cell 95(917-926)1998.

Claims 7-11, 17-21, 27-31, 37-41, 47-51, 59-63, 71-75, 83-87, 95-99, 108-112, 204-208, 216-220 require that the chimeric or fused nucleic acid molecule only comprise at least a part of the coding sequence contained in the DNA of SEQ ID NO: 20. This limitation reads on any chimeric or fused nucleic because the parts of the coding sequence of SEQ ID NO: 20 are simply A, T, G, or C. Krautwurst et al. disclose a fusion protein comprising a nucleic acid encoding an olfactory receptor (GPCR) fused to a nucleic acid sequence encoding a mammalian rhodopsin (heterologous GPCR), wherein such rhodopsin gene product helps facilitate expression of the fusion protein to the cell surface (pg 918 col 1), wherein the rhodopsin gene product further provides a detectable marker (pg 918 col 2). Such fused nucleic acid is produced with a constitutively active promoter (page 924, col 2). Claims 103-115 and 117 require a variant of SEQ ID NO: 21 containing at least one conservative substitution. Absent evidence to the contrary this reads on any polypeptide.

Claims 1, 4-7, 9, 11, 14-17, 19, 21-27, 29, 31-37, 39, 41, 44-46, 56-58, 66-171, 73, 75-83, 85, 87-89, 103-115, 117, 201-204, 206, 208-217, 218, 220-222 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Application Publication No: 203/0036089, which is fully supported by U.S. Provisional Application No: 60/172,600, filed 12/20/1999

U.S. Patent Application Publication No: 203/0036089 discloses polynucleotides, cDNA, genomic DNA , and expressed RNA [0049], wherein the polynucleotides have 95% identity with the polynucleotide of SEQ ID NO: 20 over the entire length of SEQ ID NO: 20 see attached sequence alignment, and would thus be expected to hybridize to the instant SEQ ID NO: 20 under conditions listed in the specification as stringent, although the polynucleotide is not asserted to be a active in taste signaling. Fusion proteins to facilitate purification or expression are also contemplated [0071], as well as probes and primers of about 12-50 nucleotides [0151].

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 7-11, 27-31, 37-41, 71-75, 83-87, 95-99, 109-112, 216-220 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoon *et al., Cell* 96(541-551), February 19, 1999 in view of Krautwurst et al. Cell 95(917-926)1998.

As set forth above Hoon et al. disclose a polynucleotide encoding a polypeptide with over 70% sequence identity with the instant SEQ ID NO: 20, see attached sequence alignment, and would thus be expected to hybridize under what could be considered stringent hybridization conditions as stated in the claims, absent evidence to the contrary. Hoon et al. teach that this polynucleotide is difficult to express and explicitly recommend that the expression system of Krautwurst et al. be employed to express the protein, see col 1 of page 547 of Hoon et al.

Krautwurst et al. disclose an expression system producing a fusion protein from a nucleic acid encoding an olfactory receptor (GPCR) fused to a nucleic acid sequence encoding a mammalian rhodopsin (heterologous GPCR), wherein such rhodopsin gene product helps facilitate expression of the fusion protein to the cell surface (pg 918 col 1), wherein the rhodopsin gene product further provides a detectable marker (pg 918 col 2). Such fused nucleic acid is produced with a constitutively active promoter (page 924, col 2).

Therefore, one of ordinary skill in the art, at the time the invention was made, and with reasonable expectation of success, would be motivated to make a chimeric construct with the polynucleotide of Hoon et al. and the rhodopsin construct as taught by Krautwurst et al. The motivation to do so is provided by Hoon et al. who specifically teach to do this.

Allowable Subject Matter

Claims 12, 13, 42, 43, 52-55, 65, 65, 199, 200, 209, 210 are allowable with respect to SEQ ID NO: 20 and 21, yet the claims are objected to because they contain non-elected subject matter.

Conclusion

Please note the new central fax number for official correspondence below:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, Ph.D., can be reached at (571) 272-0961. Official papers filed by fax should be directed to 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

December 11, 2004

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

```
Q9Z0R7
ID   Q9Z0R7      PRELIMINARY;      PRT;   843 AA.
AC   Q9Z0R7;
DT   01-MAY-1999 (TrEMBLrel. 10, Created)
DT   01-MAY-1999 (TrEMBLrel. 10, Last sequence update)
DT   01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE   Putative taste receptor TR2 (Fragment).
OS   Rattus norvegicus (Rat).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OX   NCBI_TaxID=10116;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=Wistar;
RX   MEDLINE=99159821; PubMed=10052456;
RA   Hoon M.A., Adler E., Lindemeier J., Battey J.F., Ryba N.J.,
RA   Zuker C.S.;
RT   "Putative mammalian taste receptors: a class of taste-specific GPCRs
RT   with distinct topographic selectivity.";
RL   Cell 96:541-551(1999).
DR   EMBL; AF127390; AAD18070.1; -.
DR   GO; GO:0016020; C:membrane; IEA.
DR   GO; GO:0008067; F:metabotropic glutamate, GABA-B-like recepto. . .; IEA.
DR   GO; GO:0004872; F:receptor activity; IEA.
DR   InterPro; IPR001828; ANF_receptor.
DR   InterPro; IPR000337; GPCR_Mgr.
DR   InterPro; IPR011500; NCD3G_GPCR.
DR   Pfam; PF00003; 7tm_3; 2.
DR   Pfam; PF01094; ANF_receptor; 1.
DR   Pfam; PF07562; NCD3G; 1.
DR   PRINTS; PR00248; GPCRMGR.
DR   PROSITE; PS50259; G_PROTEIN_RECEP_F3_4; 1.
KW   Receptor.
FT   NON_TER     843     843
SQ   SEQUENCE   843 AA;  95799 MW;  D23AC22D21E049B8 CRC64;

  Query Match            72.7%;  Score 3231;  DB 2;  Length 843;
  Best Local Similarity  70.8%;  Pred. No. 3.3e-231;
  Matches  596;  Conservative  109;  Mismatches  133;  Indels    4;  Gaps    2;

Qy          1 MGPRAKTICSLFFLLWVLAEP---AENSDFYLPGDYLLGGLFSLHANMKGIVHLNFLQVP 57
              |||:|:|:| |  || || :|    |||||:| |||||||||:||||:| | ||::||||
Db          1 MGPQARTLCLLSLLLHVLPKPGKLVENSDFHLAGDYLLGGLFTLHANVKSISHLSYLQVP 60

Qy         58 MCKEYEVKVIGYNLMQAMRFAVEEINNDSSLLPGVLLGYEIVDVCYISNNVQPVLYFLAH 117
               | |: :||:|||||||||||||||| ||||||||||||:|||||:|||: | |||||
Db         61 KCNEFTMKVLGYNLMQAMRFAVEEINNCSSLLPGVLLGYEMVDVCYLSNNIHPGLYFLAQ 120

Qy        118 EDNLLPIQEDYSNYISRVVAVIGPDNSESVMTVANFLSLFLLPQITYSAISDELRDKVRF 177
              :|:|||| :||| |:  |||||||||||| :||:| || ||:||||||||||:|||  |
Db        121 DDDLLPILKDYSQYMPHVVAVIGPDNSESAITVSNILSHFLIPQITYSAISDKLRDKRHF 180

Qy        178 PALLRTTPSADHHVEAMVQLMLHFRWNWIIVLVSSDTYGRDNGQLLGERVAR-RDICIAF 236
              |::||| ||| ||:|||||||:||:||||:|||| | |||:|  || :|: :  ||||||
Db        181 PSMLRTVPSATHHIEAMVQLMVHFQWNWIVVLVSDDDYGRENSHLLSQRLTKTSDICIAF 240

Qy        237 QETLPTLQPNQNMTSEERQRLVTIVDKLQQSTARVVVVFSPDLTLYHFFNEVLRQNFTGA 296
              || ||  : :| | |||:::|  |:|||:::::|||||||||:|:|| ||:|||| ||||
Db        241 QEVLPIPESSQVMRSEEQRQLDNILDKLRRTSARVVVVFSPELSLYSFFHEVLRWNFTGF 300

Qy        297 VWIASESWAIDPVLHNLTELGHLGTFLGITIQSVPIPGFSEFREWGPQAGPPPLSRTSQS 356
              |||||||||||||||||| | |||||:||| | |||||:||    : | |  : |:
Db        301 VWIASESWAIDPVLHNLTELRHTGTFLGVTIQRVSIPGFSQFRVRRDKPGYPVPNTTNLR 360

Qy        357 YTCNQECDNCLNATLSFNTILRLSGERVVYSVYSAVYAVAHALHSLLGCDKSTCTKRVVY 416
              ||||:|| ||| | ||| || ||||||||||||||||||||||| ||||::  |||: ||
Db        361 TTCNQDCDACLNTTKSFNNILILSGERVVYSVYSAVYAVAHALHRLLGCNRVRCTKQKVY 420

Qy        417 PWQLLEEIWKVNFTLLDHQIFFDPQGDVALHLEIVQWQWDRSQNPFQSVASYYPLQRQLK 476
              ||||| ||| |||||| :::||| |||: : |:|:||||| |||||||:||| |  ::|
Db        421 PWQLLREIWHVNFTLLGNRLFFDQQGDMPMLLDIIQWQWDLSQNPFQSIASYSPTSKRLT 480

Qy        477 NIQDISWHTVNNTIPMSMCSKRCQSGQKKKPVGIHVCCFECIDCLPGTFLNHTEDEYECQ 536
              | ::||:| |||:|:||||| || || || ||:| |||||:||:|||:|| : ||: |
Db        481 YINNVSWYTPNNTVPVSMCSKSCQPGQMKKSVGLHPCCFECLDCMPGTYLNRSADEFNCL 540

Qy        537 ACPNNEWSYQSETSCFKRQLVFLEWHEAPTIAVALLAALGFLSTLAILVIFWRHFQTPIV 596
              :|| : |||:: :||:|:  |||||| ||| ||:|||||| |||||| |||||||||:|
Db        541 SCPGSMWSYKNDITCFQRRPTFLEWHEVPTIVVAILAALGFFSTLAILFIFWRHFQTPMV 600

Qy        597 RSAGGPMCFLMLTLLLVAYMVVPVYVGPPKVSTCLCRQALFPLCFTICISCIAVRSFQIV 656
              |||||||||||  ||:|: :|||||||| | :| |||| | :||:||:||| |||||||
Db        601 RSAGGPMCFLMLVPLLLAFGMVPVYVGPPTVFSCFCRQAFFTVCFSICLSCITVRSFQIV 660

Qy        657 CAFKMASRFPRAYSYWVRYQGPYVSMAFITVLKMVIVVIGMLATGLSPTTRTDPDDPKIT 716
              | |||| | | |||:|:|| |||| :|||| :|: :||  |||| ::|  |||||| |
Db        661 CVFKMARRLPSAYSFWMRYHGPYVFVAFITAIKVALVVGNMLATTINPIGRTDPDDPNIM 720

Qy        717 IVSCNPNYRNSLLFNTSLDLLLSVVGFSFAYMGKELPTNYNEAKFITLSMTFYFTSSVSL 776
              |:||:||||| ||||||:|||||:|||||||||||||||||||||||||||| ||||:||
Db        721 ILSCHPNYRNGLLFNTSMDLLLSVLGFSFAYMGKELPTNYNEAKFITLSMTFSFTSSISL 780

Qy        777 CTFMSAYSGVLVTIVDLLVTVLNLLAISLGYFGPKCYMILFYPERNTPAYFNSMIQGYTM 836
              |||||| : |||||:|||||||| ||| ||||||||||||||||||| ||||||||||
Db        781 CTFMSVHDGVLVTIMDLLVTVLNFLAIGLGYFGPKCYMILFYPERNTSAYFNSMIQGYTM 840
```

RESULT 8
US-10-261-482-3
; Sequence 3, Application US/10261482
; Publication No. US20030036089A1
; GENERAL INFORMATION:
; APPLICANT: WEI, Ming-Hui et al
; TITLE OF INVENTION: ISOLATED HUMAN G-PROTEIN COUPLED
; TITLE OF INVENTION: RECEPTORS, NUCLEIC ACID MOLECULES ENCODING HUMAN GPCR
; TITLE OF INVENTION: PROTEINS, AND USES THEREOF
; FILE REFERENCE: CL000869CON
; CURRENT APPLICATION NUMBER: US/10/261,482
; CURRENT FILING DATE: 2002-10-02
; PRIOR APPLICATION NUMBER: 09/684,393
; PRIOR FILING DATE: 2000-10-10
; PRIOR APPLICATION NUMBER: 60/172,600
; PRIOR FILING DATE: 1999-12-20
; NUMBER OF SEQ ID NOS: 10
; SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 3
; LENGTH: 8001
; TYPE: DNA
; ORGANISM: Human
US-10-261-482-3

Query Match 95.5%; Score 3403.8; DB 14; Length 8001;
Best Local Similarity 97.9%; Pred. No. 0;
Matches 3489; Conservative 0; Mismatches 22; Indels 52; Gaps 2;

```
Qy          1 AGCCTGGCAGTGGCCTCAGGCAGAGTCTGACGCGCACAAACTTTCAGGCCCAGGAAGCGA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1908 AGCCTGGCAGTGGCCTCAGGCAGAGTCTGACGCGCACAAACTTTCAGGCCCAGGAAGCGA 1967

Qy         61 GGACACCACTGGGGCCCCAGGGTGTGGCAAGTGAGGATGGCAAGGGTTTTGCTAAACAAA 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1968 GGACACCACTGGGGCCCCAGGGTGTGGCAAGTGAGGATGGCAAGGGTTTTGCTAAACAAA 2027

Qy        121 TCCTCTGCCCGCTCCCCGCCCCGGGCTCACTCCATGTGAGGCCCCAGTCGGGGCAGCCAC 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2028 TCCTCTGCCCGCTCCCCGCCCCGGGCTCACTCCATGTGAGGCCCCAGTCGGGGCAGCCAC 2087

Qy        181 CTGCCGTGCCTGTTGGAAGTTGCCTCTGCCATGCTGGGCCCTGCTGTCCTGGGCCTCAGC 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2088 CTGCCGTGCCTGTTGGAAGTTGCCTCTGCCATGCTGGGCCCTGCTGTCCTGGGCCTCAGC 2147

Qy        241 CTCTGGGCTCTCCTGCACCCTGGGACGGGGGCCCCATTGTGCCTGTCACAGCAACTTAGG 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2148 CTCTGGGCTCTCCTGCACCCTGGGACGGGGGCCCCATTGTGCCTGTCACAGCAACTTAGG 2207

Qy        301 ATGAAGGGGGACTACGTGCTGGGGGGGCTGTTCCCCCTGGGCGAGGCCGAGGAGGCTGGC 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2208 ATGAAGGGGGACTACGTGCTGGGGGGGCTGTTCCCCCTGGGCGAGGCCGAGGAGGCTGGC 2267

Qy        361 CTCCGCAGCCGGACACGGCCCAGCAGCCCTGTGTGCACCAGGTACAGAGGTGGGACGGCC 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2268 CTCCGCAGCCGGACACGGCCCAGCAGCCCTGTGTGCACCAGGTACAGAGGTGGGACGGCC 2327

Qy        421 TGGGTCGGGGTCAGGGTGACCAGGTCTGGGGTGCTCCTGAGCTGGGGCCGAGGTGGCCAT 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2328 TGGGTCGGGGTCAGGGTGACCAGGTCTGGGGTGCTCCTGAGCTGGGGCCGAGGTGGCCAT 2387

Qy        481 CTGCGGTTCTGTGTGGCCCCAGGTTCTCCTCAAACGGCCTGCTCTGGGCACTGGCCATGA 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2388 CTGCGGTTCTGTGTGGCCCCAGGTTCTCCTCAAACGGCCTGCTCTGGGCACTGGCCATGA 2447

Qy        541 AAATGGCCGTGGAGGAGATCAACAACAAGTCGGATCTGCTGCCCGGGCTGCGCCTGGGCT 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2448 AAATGGCCGTGGAGGAGATCAACAACAAGTCGGATCTGCTGCCCGGGCTGCGCCTGGGCT 2507

Qy        601 ACGACCTCTTTGATACGTGCTCGGAGCCTGTGGTGGCCATGAAGCCCAGCCTCATGTTCC
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2508 ACGACCTCTTTGATACGTGCTCGGAGCCTGTGGTGGCCATGAAGCCCAGCCTCATGTTCC

Qy        661 TGGCCAAGGCAGGCAGCCGCGACATCGCCGCCTACTGCAACTACACGCAGTACCAGCCCC
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2568 TGGCCAAGGCAGGCAGCCGCGACATCGCCGCCTACTGCAACTACACGCAGTACCAGCCCC

Qy        721 GTGTGCTGGCTGTCATCGGGCCCCACTCGTCAGAGCTCGCCATGGTCACCGGCAAGTTCT
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2628 GTGTGCTGGCTGTCATCGGGCCCCACTCGTCAGAGCTCGCCATGGTCACCGGCAAGTTCT

Qy        781 TCAGCTTCTTCCTCATGCCCCAGTGGGGCGCCCCCCACCATCACCCACCCCCAACCAACC
              |||||||||||||||||||||  ||||||||||||||||||||||||||| ||| ||
Db       2688 TCAGCTTCTTCCTCATGCCCCAGGTGGGCGCCCCCCACCATCACCCACCCCCACCCAGCC

Qy        841 CCTGCCCCGTGGGAGCCCCTTGTGTCAGGAGAATGCTACATGCACCCCACCCAGCCCTGC
              |   ||  | | |   ||| ||||||||||||   ||
Db       2748 CTGCCCGTGGGAG---CCCCTGTGTCAGGAGATGCCT----------------------

Qy        901 CCTGGGAGCCCTGTGTCAGAAGATGCTCTTGGCCTTGCAGGTCAGCTACGGTGCTAGCAT
                                    | | ||||||||||||||||||||||||||||||
Db       2782 -------------------------CTTGGCCCTTGCAGGTCAGCTACGGTGCTAGCAT

Qy        961 GGAGCTGCTGAGCGCCCGGGAGACCTTCCCCTCCTTCTTCCGCACCGTGCCCAGCGACCG
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2816 GGAGCTGCTGAGCGCCCGGGAGACCTTCCCCTCCTTCTTCCGCACCGTGCCCAGCGACCG

Qy       1021 TGTGCAGCTGACGGCCGCCGCGGAGCTGCTGCAGGAGTTCGGCTGGAACTGGGTGGCCGC
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2876 TGTGCAGCTGACGGCCGCCGCGGAGCTGCTGCAGGAGTTCGGCTGGAACTGGGTGGCCGC

Qy       1081 CCTGGGCAGCGACGACGAGTACGGCCGGCAGGGCCTGAGCATCTTCTCGGCCCTGGCCGC
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2936 CCTGGGCAGCGACGACGAGTACGGCCGGCAGGGCCTGAGCATCTTCTCGGCCCTGGCCGC

Qy       1141 GGCACGCGGCATCTGCATCGCGCACGAGGGCCTGGTGCCGCTGCCCCGTGCCGATGACTC
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       2996 GGCACGCGGCATCTGCATCGCGCACGAGGGCCTGGTGCCGCTGCCCCGTGCCGATGACTC

Qy       1201 GCGGCTGGGGAAGGTGCAGGACGTCCTGCACCAGGTGAACCAGAGCAGCGTGCAGGTGGT
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3056 GCGGCTGGGGAAGGTGCAGGACGTCCTGCACCAGGTGAACCAGAGCAGCGTGCAGGTGGT

Qy       1261 GCTGCTGTTCGCCTCCGTGCACGCCGCCCACGCCCTCTTCAACTACAGCATCAGCAGCAG
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3116 GCTGCTGTTCGCCTCCGTGCACGCCGCCCACGCCCTCTTCAACTACAGCATCAGCAGCAG

Qy       1321 GCTCTCGCCCAAGGTGTGGGTGGCCAGCGAGGCCTGGCTGACCTCTGACCTGGTCATGGG
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3176 GCTCTCGCCCAAGGTGTGGGTGGCCAGCGAGGCCTGGCTGACCTCTGACCTGGTCATGGG

Qy       1381 GCTGCCCGGCATGGCCCAGATGGGCACGGTGCTTGGCTTCCTCCAGAGGGGTGCCCAGCT
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3236 GCTGCCCGGCATGGCCCAGATGGGCACGGTGCTTGGCTTCCTCCAGAGGGGTGCCCAGCT

Qy       1441 GCACGAGTTCCCCCAGTACGTGAAGACGCACCTGGCCCTGGCCACCGACCCGGCCTTCTG
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3296 GCACGAGTTCCCCCAGTACGTGAAGACGCACCTGGCCCTGGCCACCGACCCGGCCTTCTG

Qy       1501 CTCTGCCCTGGGCGAGAGGGAGCAGGGTCTGGAGGAGGACGTGGTGGGCCAGCGCTGCCC
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3356 CTCTGCCCTGGGCGAGAGGGAGCAGGGTCTGGAGGAGGACGTGGTGGGCCAGCGCTGCCC

Qy       1561 GCAGTGTGACTGCATCACGCTGCAGAACGTGAGCGCAGGGCTAAATCACCACCAGACGTT
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3416 GCAGTGTGACTGCATCACGCTGCAGAACGTGAGCGCAGGGCTAAATCACCACCAGACGTT

Qy       1621 CTCTGTCTACGCAGCTGTGTATAGCGTGGCCCAGGCCCTGCACAACACTCTTCAGTGCAA
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3476 CTCTGTCTACGCAGCTGTGTATAGCGTGGCCCAGGCCCTGCACAACACTCTTCAGTGCAA
```

```
1681 CGCCTCAGGCTGCCCCGCGCAGGACCCCGTGAAGCCCTGGCAGGTGAGCCCGGGAGATGG 1740
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
3536 CGCCTCAGGCTGCCCCGCGCAGGACCCCGTGAAGCCCTGGCAGGTGAGCCCGGGAGATGG 3595

1741 GGGTGTGCTGTCCTCTGCATGTGCCCAGGCCACCAGGCACGGCCACCACGCCTGAGCTGG 1800
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
3596 GGGTGTGCTGTCCTCTGCATGTGCCCAGGCCACCAGGCACGGCCACCACGCCTGAGCTGG 3655

1801 AGGTGGCTGGCGGCTCAGCCCCGTCCCCCGCCCGCAGCTCCTGGAGAACATGTACAACCT 1860
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
3656 AGGTGGCTGGCGGCTCAGCCCCGTCCCCCGCCCGCAGCTCCTGGAGAACATGTACAACCT 3715

1861 GACCTTCCACGTGGGCGGGCTGCCGCTGCGGTTCGACAGCAGCGGAAACGTGGACATGGA 1920
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
3716 GACCTTCCACGTGGGCGGGCTGCCGCTGCGGTTCGACAGCAGCGGAAACGTGGACATGGA 3775

1921 GTACGACCTGAAGCTGTGGGTGTGGCAGGGCTCAGTGCCCAGGCTCCACGACGTGGGCAG 1980
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
3776 GTACGACCTGAAGCTGTGGGTGTGGCAGGGCTCAGTGCCCAGGCTCCACGACGTGGGCAG 3835

1981 GTTCAACGGCAGCCTCAGGACAGAGCGCCTGAAGATCCGCTGGCACACGTCTGACAACCA 2040
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
3836 GTTCAACGGCAGCCTCAGGACAGAGCGCCTGAAGATCCGCTGGCACACGTCTGACAACCA 3895

2041 GGTGAGGTGAGGGTGGGTGTGCCAGGCGTGCCCGTGGTAGCCCCCGCGGCAGGGCGCAGC 2100
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
3896 GGTGAGGTGAGGGTGGGTGTGCCAGGCGTGCCCGTGGTAGCCCCCGCGGCAGGGCGCAGC 3955

2101 CTGGGGGTGGGGGCCGTTCCAGTCTCCCGTGGGCATGCCCAGCCGAGCAGAGCCAGACCC 2160
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
3956 CTGGGGGTGGGGGCCGTTCCAGTCTCCCGTGGGCATGCCCAGCCGAGCAGAGCCAGACCC 4015

2161 CAGGCCTGTGCGCAGAAGCCCGTGTCCCGGTGCTCGCGGCAGTGCCAGGAGGGCCAGGTG 2220
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
4016 CAGGCCTGTGCGCAGAAGCCCGTGTCCCGGTGCTCGCGGCAGTGCCAGGAGGGCCAGGTG 4075

2221 CGCCGGGTCAAGGGGTTCCACTCCTGCTGCTACGACTGTGTGGACTGCGAGGCGGGCAGC 2280
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
4076 CGCCGGGTCAAGGGGTTCCACTCCTGCTGCTACGACTGTGTGGACTGCGAGGCGGGCAGC 4135

2281 TACCGGCAAAACCCAGGTGAGCCGCCTTCCCGGCAGGCGGGGGTGGGAACGCAGCAGGGG 2340
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
4136 TACCGGCAAAACCCAGGTGAGCCGCCTTCCCGGCAGGCGGGGGTGGGAACGCAGCAGGGG 4195

2341 AGGGTCCTGCCAAGTCCTGACTCTGAGACCAGAGCCCACAGGGTACAAGACGAACACCCA 2400
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
4196 AGGGTCCTGCCAAGTCCTGACTCTGAGACCAGAGCCCACAGGGGACAAGACGAACACCCA 4255

2401 GCGCCCTTCTCCTCTCTCACAGACGACATCGCCTGCACCTTTTGTGGCCAGGATGAGTGG 2460
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
4256 GCGCCCTTCTCCTCTCTCACAGACGACATCGCCTGCACCTTTTGTGGCCAGGATGAGTGG 4315

2461 TCCCCGGAGCGAAGCACACGCTGCTTCCGCCGCAGGTCTCGGTTCCTGGCATGGGGCGAG 2520
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
4316 TCCCCGGAGCGAAGCACACGCTGCTTCCGCCGCAGGTCTCGGTTCCTGGCATGGGGCGAG 4375

2521 CCGGCTGTGCTGCTGCTGCTCCTGCTGCTGAGCCTGGCGCTGGGCCTTGTGCTGGCTGCT 2580
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
4376 CCGGCTGTGCTGCTGCTGCTCCTGCTGCTGAGCCTGGCGCTGGGCCTTGTGCTGGCTGCT 4435

2581 TTGGGGCTGTTCGTTCACCATCGGGACAGCCCACTGGTTCAGGCCTCGGGGGGGCCCCTG 2640
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
4436 TTGGGGCTGTTCGTTCACCATCGGGACAGCCCACTGGTTCAGGCCTCGGGGGGGCCCCTG 4495

2641 GCCTGCTTTGGCCTGGTGTGCCTGGGCCTGGTCTGCCTCAGCGTCCTCCTGTTCCCTGGC 2700
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
4496 GCCTGCTTTGGCCTGGTGTGCCTGGGCCTGGTCTGCCTCAGCGTCCTCCTGTTCCCTGGC 4555

2701 CAGCCCAGCCCTGCCCGATGCCTGGCCCAGCAGCCCTTGTCCCACCTCCCGCTCACGGGC 2760
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
4556 CAGCCCAGCCCTGCCCGATGCCTGGCCCAGCAGCCCTTGTCCCACCTCCCGCTCACGGGC 4615

2761 TGCCTGAGCACACTCTTCCTGCAGGCGGCCGAGATCTTCGTGGAGTCAGAACTGCCTCTG 2820
```

```
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   4616 TGCCTGAGCACACTCTTCCTGCAGGCGGCCGAGATCTTCGTGGAGTCAGAACTGCCTCTG 4675

Qy   2821 AGCTGGGCAGACCGGCTGAGTGGCTGCCTGCGGGGGCCCTGGGCCTGGCTGGTGGTGCTG 2880
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   4676 AGCTGGGCAGACCGGCTGAGTGGCTGCCTGCGGGGGCCCTGGGCCTGGCTGGTGGTGCTG 4735

Qy   2881 CTGGCCATGCTGGTGGAGGTCGCACTGTGCACCTGGTACCTGGTGGCCTTCCCGCCGGAG 2940
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   4736 CTGGCCATGCTGGTGGAGGTCGCACTGTGCACCTGGTACCTGGTGGCCTTCCCGCCGGAG 4795

Qy   2941 GTGGTGACGGACTGGCACATGCTGCCCACGGAGGCGCTGGTGCACTGCCGCACACGCTCC 3000
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   4796 GTGGTGACGGACTGGCACATGCTGCCCACGGAGGCGCTGGTGCACTGCCGCACACGCTCC 4855

Qy   3001 TGGGTCAGCTTCGGCCTAGCGCACGCCACCAATGCCACGCTGGCCTTTCTCTGCTTCCTG 3060
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   4856 TGGGTCAGCTTCGGCCTAGCGCACGCCACCAATGCCACGCTGGCCTTTCTCTGCTTCCTG 4915

Qy   3061 GGCACTTTCCTGGTGCGGAGCCAGCCGGGCTGCTACAACCGTGCCCGTGGCCTCACCTTT 3120
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   4916 GGCACTTTCCTGGTGCGGAGCCAGCCGGGCCGCTACAACCGTGCCCGTGGCCTCACCTTT 4975

Qy   3121 GCCATGCTGGCCTACTTCATCACCTGGGTCTCCTTTGTGCCCCTCCTGGCCAATGTGCAG 3180
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   4976 GCCATGCTGGCCTACTTCATCACCTGGGTCTCCTTTGTGCCCCTCCTGGCCAATGTGCAG 5035

Qy   3181 GTGGTCCTCAGGCCCGCCGTGCAGATGGGCGCCCTCCTGCTCTGTGTCCTGGGCATCCTG 3240
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   5036 GTGGTCCTCAGGCCCGCCGTGCAGATGGGCGCCCTCCTGCTCTGTGTCCTGGGCATCCTG 5095

Qy   3241 GCTGCCTTCCACCTGCCCAGGTGTTACCTGCTCATGCGGCAGCCAGGGCTCAACACCCCC 3300
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   5096 GCTGCCTTCCACCTGCCCAGGTGTTACCTGCTCATGCGGCAGCCAGGGCTCAACACCCCC 5155

Qy   3301 GAGTTCTTCCTGGGAGGGGGCCCTGGGGATGCCCAAGGCCAGAATGACGGGAACACAGGA 3360
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   5156 GAGTTCTTCCTGGGAGGGGGCCCTGGGGATGCCCAAGGCCAGAATGACGGGAACACAGGA 5215

Qy   3361 AATCAGGGGAAACATGAGTGACCCAACCCTGTGATCTCAGCCCCGGTGAACCCAGACTTA 3420
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   5216 AATCAGGGGAAACATGAGTGACCCAACCCTGTGATCTCAGCCCCGGTGAACCCAGACTTA 5275

Qy   3421 GCTGCGATCCCCCCCAAGCCAGCAATGACCCGTGTCTCGCTACAGAGACCCTCCCGCTCT 3480
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   5276 GCTGCGATCCCCCCCAAGCCAGCAATGACCCGTGTCTCGCTACAGAGACCCTCCCGCTCT 5335

Qy   3481 AGGTTCTGACCCCAGGTTGTCTCCTGACCCTGACCCCACAGTGAGCCCTAGGCCTGGAGC 3540
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   5336 AGGTTCTGACCCCAGGTTGTCTCCTGACCCTGACCCCACAGTAAGCCCTAGGCCTGGAGC 5395

Qy   3541 ACGTGGACACCCCTGTGACCATC 3563
     |||||||||||||||||||||||
Db   5396 ACGTGGACACCCCTGTGACCATC 5418
```